09/917,215

June 17,2002

=> d que		
L1	10	SEA FILE=REGISTRY ABB=ON PLU=ON ("PROSTAGLANDIN EP3 RECEPTOR (HUMAN ISOFORM VI)"/CN OR "PROSTAGLANDIN EP3 RECEPTOR (SWINE CLONE P6917)"/CN OR "PROSTAGLANDIN EP3 RECEPTOR (SWINE)"/CN OR "PROSTAGLANDIN EP3.ALPHA. RECEPTOR (RAT KIDNEY CLONE PREP3)"/CN OR "PROSTAGLANDIN EP3.ALPHA. RECEPTOR (RATTUS NORVEGICUS CLONE 15/2)"/CN OR "PROSTAGLANDIN EP3A RECEPTOR (OX ADRENAL MEDULLA)"/CN OR "PROSTAGLANDIN EP3B RECEPTOR (OX ADRENAL MEDULLA)"/CN OR "PROSTAGLANDIN EP3C RECEPTOR (OX ADRENAL MEDULLA)"/CN OR "PROSTAGLANDIN EP3D RECEPTOR (OX ADRENAL MEDULLA)"/CN OR "PROSTAGLANDIN EP3D RECEPTOR (RATTUS NORVEGICUS)"/CN)
ĽŽ		SEA FILE=REGISTRY ABB=ON PLU=ON ("PROSTAGLANDIN EP2 RECEPTOR (DOG CLONE B3A)"/CN OR "PROSTAGLANDIN EP2 RECEPTOR (HUMAN LUNG)"/CN OR "PROSTAGLANDIN EP2 RECEPTOR (MOUSE CLONE MP412)"/CN OR "PROSTAGLANDIN EP2 RECEPTOR (RATTUS NORVEGICUS CLONE .LAMBDA.19A1)"/CN OR "PROSTAGLANDIN EP2 RECEPTOR (RATTUS NORVEGICUS CLONE SJ26)"/CN)
L3		SEA FILE=REGISTRY ABB=ON PLU=ON ("PROSTAGLANDIN EP4 RECEPTOR (DOG CLONE N8D 356-AMINO ACID C-TERMINAL TRUNCATED FRAGMENT)"/C N OR "PROSTAGLANDIN EP4 RECEPTOR (DOG CLONE N8D)"/CN OR "PROSTAGLANDIN EP4 RECEPTOR (HUMAN REDUCED)"/CN OR "PROSTAGLANDIN EP4 RECEPTOR (RATTUS NORVEGICUS CLONE 3/4)"/CN)
L7	303	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L) EP3"+OLD/CT
L8	250	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L) EP4"+OLD/CT
L9	289	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L) EP2"+OLD/CT
L15	7405	SEA FILE=HCAPLUS ABB=ON PLU=ON "DRUG DELIVERY SYSTEMS (L) TOPICAL"+OLD/CT
L16	650	SEA FILE=HCAPLUS ABB=ON PLU=ON "DRUG DELIVERY SYSTEMS (L) GELS, TOPICAL"+OLD/CT
L17		SEA FILE=HCAPLUS ABB=ON PLU=ON "DRUG DELIVERY SYSTEMS (L) EMULSIONS, TOPICAL"+OLD/CT
L18	209	SEA FILE=HCAPLUS ABB=ON PLU=ON "DRUG DELIVERY SYSTEMS (L) EMULSIONS, TOPICAL"+OLD/CT
L20	266	SEA FILE=HCAPLUS ABB=ON PLU=ON "DRUG DELIVERY SYSTEMS (L) SOLNS., TOPICAL"+OLD/CT
L22	7405	SEA FILE=HCAPLUS ABB=ON PLU=ON (L15 OR L16 OR L17 OR L18) OR L20
L23	1	SEA FILE=HCAPLUS ABB=ON PLU=ON ((L1 OR L2 OR L3) OR (L7 OR L8 OR L9)) AND L22

```
L23 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
AN
    2000:456890 HCAPLUS
DN
    133:79365
TΙ
    Prostaglandin E agonists for treatment of dry eye
IN
    Klimko, Peter G.
PΑ
    Alcon Laboratories, Inc., USA
SO
    PCT Int. Appl., 28 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
FAN.CNT 1
    PATENT NO.
                    KIND DATE
                                         APPLICATION NO. DATE
    -----
                    ----
                                         ______
    WO 2000038690 A2 20000706
WO 2000038690 A3 20001123
                           20000706
PI
                                         WO 1999-US29733 19991214
        W: AU, BR, CA, JP, MX, US
        RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
            PT, SE
PRAI US 1998-113574P
                    P 19981224
os
    MARPAT 133:79365
AΒ
    Compns. and methods for the treatment of dry eye and related diseases in
    mammals utilizing prostaglandin E receptor agonists are disclosed.
IC
    ICM A61K031-557
CC
    63-6 (Pharmaceuticals)
    Section cross-reference(s): 1
ΙT
    Prostanoid receptors
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (EP4, agonists; prostaglandin E agonists for treatment of dry
       eye)
IT
    Drug delivery systems
        (topical; prostaglandin E agonists for treatment of dry eye)
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June 17, 2002

=> d que			
L1	1330		OWTH
_		STIMULANTS"/CT	
L5	97	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
		EP"+OLD/CT	
L6	289	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
•		EP2"+OLD/CT	
L7	303	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
		EP3"+OLD/CT	
L8	16	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
		EP3.ALPHA."+OLD/CT	
L9	17	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	•
ш		EP3.BETA."+OLD/CT	
L10	2	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
пто	3		
+ 1 1	_	EP3.GAMMA."+OLD/CT	
L11	Z	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
		EP3C"+OLD/CT	
L12	4	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
		EP3D"+OLD/CT	
L13	250	SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTANOID RECEPTORS (L)	
	·	EP4"+OLD/CT	
L14	635	SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 OR L6 OR L7 OR L8 OR 1	L9
		OR L10 OR L11 OR L12 OR L13)	
L15		SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND L14	

```
L15 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
    2001:730519 HCAPLUS
AN
     135:267274
DN
     prostaglandin EP4 receptor agonists for controlling hair growth
ΤI
     Kumagai, Hiroki; Yamada, Naohiro; Hayashi, Ryoji; Mori, Takeshi; Isogaya,
     Masafumi
     Toray Industries, Inc., Japan
PA
     PCT Int. Appl., 79 pp.
SO
     CODEN: PIXXD2
     Patent
DT
     Japanese
LA
FAN.CNT 1
                                           APPLICATION NO.
     PATENT NO.
                      KIND DATE
                                                            DATE
                                           -----
     -----
                     ____
                            _____
                            20011004
                                           WO 2001-JP2756
                                                            20010330
PΙ
     WO 2001072268
                      A1
        W: AU, CA, CN, JP, KR, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     EP 1186287
                      A1
                            20020313
                                           EP 2001-917702
                                                            20010330
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
PRAI JP 2000-97542
                            -20000331
                       Α
                            20010330
     WO 2001-JP2756
                       W
OS
     MARPAT 135:267274
     Disclosed are agents for controlling hair growth or hair formation while
AΒ
     showing little side effect. These agents contain 5,6,7-trinor-4,8-inter-m-
     phenylene PGI2 derivs. as prostaglandin EP4 receptor agonists. Hair
     growth-promoting activities of the compds. were tested with rabbits.
IC
     ICM A61K007-06
     ICS A61P017-14
     1-12 (Pharmacology)
CC
     Section cross-reference(s): 62
TT
     Prostanoid receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (EP4; prostaglandin EP4 receptor agonists for
        controlling hair growth)
IT
     Hair preparations
        (growth stimulants; prostaglandin EP4 receptor
        agonists for controlling hair growth)
              THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
       13
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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09/917,215

June 17, 2002

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=> d que
L17 764 SEA FILE=MEDLINE ABB=ON PLU=ON "RECEPTORS, PROSTAGLANDIN
E"/CT
L18 813 SEA FILE=MEDLINE ABB=ON PLU=ON L17 OR PROSTAGLANDIN(3A)(EP2
OR EP3 OR EP 4 OR EP4 OR EP 2 OR EP 3)
L21 2 SEA FILE=MEDLINE ABB=ON PLU=ON L18 AND HAIR?
```

=> d bib ab hitind 1-2

- L21 ANSWER 1 OF 2 MEDLINE
- AN 2002060591 MEDLINE
- DN 21645891 PubMed ID: 11785955
- TI Expression of prostaglandin E(2) receptor subtypes in mouse hair follicles.
- AU Torii Eiko; Segi Eri; Sugimoto Yukihiko; Takahashi Kenzo; Kabashima Kenji; Ikai Kohichi; Ichikawa Atsushi
- CS Department of Physiological Chemistry, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, 606-8501, Japan.
- BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2002 Jan 18) 290 (2) 696-700.
 - Journal code: 0372516. ISSN: 0006-291X.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200202
- ED Entered STN: 20020125 Last Updated on STN: 20020212 Entered Medline: 20020211
- We investigated the mRNA distribution of the prostaglandin (PG) E(2) AΒ receptor subtypes and cyclooxygenases (COXs) in hair follicles of the mouse dorsal skin. In the 3-week hair follicles, which are in the anagen phase, EP3 and EP4 mRNA were expressed in the dermal papilla cells and the outer root sheath cells located in the hair bulb region, respectively. In the 8-week hair follicles, which are in the telogen phase, the signals for both EP3 and EP4 mRNAs had disappeared. To study the hair cycle-dependent expression of mRNAs for the EPs and COXs, an area of dorsal hair was depilated from 8-week-old mice. On days 8 and 12 after depilation, EP3 and EP4 mRNA were reexpressed in the dermal papilla cells and the outer root sheath cells, and the induction of COX-2 mRNA was also observed in the outer root sheath cells, the upper area of EP4 expression site. These results suggest that EP3 and EP4 receptors may involve in the development and regrowth of the hair follicles.
- CT Check Tags: Animal; Male; Support, Non-U.S. Gov't

Enzyme Induction: PH, physiology

Hair Follicle: CY, cytology
*Hair Follicle: ME, metabolism

In Situ Hybridization

Isoenzymes: BI, biosynthesis
Isoenzymes: GE, genetics

Mice

Mice, Inbred C57BL

Prostaglandin-Endoperoxide Synthase: BI, biosynthesis Prostaglandin-Endoperoxide Synthase: GE, genetics

*RNA, Messenger: BI, biosynthesis

*Receptors, Prostaglandin E: BI, biosynthesis Receptors, Prostaglandin E: GE, genetics

- CN 0 (Isoenzymes); 0 (RNA, Messenger); 0 (Receptors, Prostaglandin E); EC 1.14.99.- (cyclooxygenase 1); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)
- L21 ANSWER 2 OF 2 MEDLINE
- AN 2001298131 MEDLINE
- DN 21273355 PubMed ID: 11376908
- TI Topical bicuculline to the rat spinal cord induces highly localized allodynia that is mediated by spinal prostaglandins.
- AU Zhang Z; Hefferan M P; Loomis C W
- CS School of Pharmacy and Division of Basic Medical Sciences, Faculty of Medicine, Memorial University of Newfoundland, St. John's, A1B 3V6, Newfoundland, Canada.
- SO PAIN, (2001 Jun) 92 (3) 351-61. Journal code: 7508686. ISSN: 0304-3959.
- CY Netherlands
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200108
- ED Entered STN: 20010903
 Last Updated on STN: 20010903
 Entered Medline: 20010830
- Entered Medline: 20010830 The purpose of this study was to investigate the allodynic effect of AΒ bicuculline (BIC) given topically to the dorsal surface of the rat spinal cord, and to determine if spinal prostaglandins (PGs) mediate the allodynic state arising from spinal GABA(A)-receptor blockade. Male Sprague-Dawley rats (325-400 g) were anaesthetized with halothane and maintained with urethane for the continuous monitoring of blood pressure (MAP), heart rate (HR) and cortical electroencephalogram (EEG). A laminectomy was performed to expose the dorsal surface of the spinal cord. Unilateral application of BIC (0.1 microg in 0.1 microl) to the L5 or L6 spinal segment induced a highly localized allodynia (e.g. one or two digits) on the ipsilateral hind paw. Thus, hair deflection (brushing the hair with a cotton-tipped applicator) in the presence, but not absence of BIC, evoked an increase in MAP and HR, abrupt motor responses (MR; e.g. withdrawal of the hind leg, kicking, and/or scratching) on the affected side, and desynchrony of the EEG. BIC-allodynia was dose-dependent, yielding ED(50)'s (95% CI's) of 45 ng (31-65) for MAP; 68 ng (46-101) for HR and 76 ng (60-97) for MR. Allodynia was sustained for up to 2 h with repeated BIC application without any detectable change in the location or area of peripheral sensitization. Pretreatment with either the EP(1) - receptor antagonist, SC-51322, the cyclooxygenase (COX)-2 selective inhibitor, NS-398, or the NMDA-receptor antagonist, AP-7, inhibited BIC-allodynia in a dose-dependent manner. The results demonstrate: (a) BIC, applied to the dorsal surface of the spinal cord, induces highly localized allodynia; (b) this effect can be sustained with repeated BIC application; (c) it is evoked by NMDA-dependent afferent input; (d) spinal PGs are synthesized by constitutive COX-2 during BIC-allodynia; and (e) spinal PGs contribute to the abnormal processing of tactile input via spinal EP1-receptors.
- CT Check Tags: Animal; Male; Support, Non-U.S. Gov't 2-Amino-5-phosphonovalerate: AA, analogs & derivatives 2-Amino-5-phosphonovalerate: PD, pharmacology

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Administration, Topical
*Bicuculline: PD, pharmacology
 Blood Pressure: DE, drug effects
 Blood Pressure: PH, physiology
 Cyclooxygenase Inhibitors: PD, pharmacology
 Dose-Response Relationship, Drug
 Electroencephalography: DE, drug effects
 Excitatory Amino Acid Antagonists: PD, pharmacology
*GABA Antagonists: PD, pharmacology
 Heart Rate: DE, drug effects
 Heart Rate: PH, physiology
Motor Neurons: DE, drug effects
Motor Neurons: PH, physiology
Nitrobenzenes: PD, pharmacology
*Pain Measurement: DE, drug effects
Pain Measurement: MT, methods
*Posterior Horn Cells: DE, drug effects
Posterior Horn Cells: PH, physiology
*Prostaglandins: ME, metabolism
 Rats
 Rats, Sprague-Dawley
  Receptors, Prostaglandin E: AI, antagonists & inhibitors
 Spinal Cord: DE, drug effects
 Spinal Cord: PH, physiology
 Sulfonamides: PD, pharmacology
*Touch: DE, drug effects
Touch: PH, physiology
123653-11-2 (NS 398); 485-49-4 (Bicuculline); 76726-92-6
(2-Amino-5-phosphonovalerate); 85797-13-3 (2-amino-7-phosphonoheptanoic
acid)
0 (Cyclooxygenase Inhibitors); 0 (Excitatory Amino Acid Antagonists); 0
(GABA Antagonists); 0 (Nitrobenzenes); 0 (Prostaglandins); 0 (Receptors,
Prostaglandin E); 0 (Sulfonamides); 0 (prostanoid receptor EP1)
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CN